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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,755	01/28/2004	Gregory L. Stahl	A0752.70001US01	2264

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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

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07/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,755	STAHL ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2006 and 02 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *4,39,42 and 75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-22,24,30-36,38,40,41,43-54 and 56-67* is/are rejected.

7)☒ Claim(s) *23, 25-29, 37, 55 and 68-74* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20040804*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a divisional of U.S. Application Serial Number 09/464,303, which claims the benefit of the filing date of provisional U.S. Application 60/112,390.

Claims 1-75 are currently pending.

Election/Restrictions

1. Claim 75 was erroneously included with the inventions of Group II in the restriction requirement mailed October 12, 2006. As a method of screening, it should have been included in Group III, but not in Groups I or II.

2. Applicant's election with traverse of Group II, claims 14, 18-29, 31, 34-37, 52-55, 61, and 63-74 as they read upon a method for inhibiting lectin complement pathway associated complement activation comprising administering an MBL binding antibody or antibody fragment in the reply filed on December 14, 2006 is acknowledged.

Note that claims 1-13, 15-17, 30, 32, 33, 38, 40-51, 56-60, and 62 are linking claims that link the inventions of Groups I and II and will be examined here with the invention of Group II.

Applicant's election with traverse of the species "myocardial infarction," readable on claims 1-3, 5-38, 40, 41, 43-74 as they read upon a method for inhibiting lectin complement pathway associated complement activation comprising administering an MBL binding antibody or antibody fragment in the reply filed on December 14, 2006 is acknowledged.

The traversal is on the ground(s) that it would not cause serious burden for the Examiner to search the inventions of all three groups at the same time. This is not found persuasive because antibodies and non-antibody inhibitors of MBL are structurally different, have different binding properties and require extensively different search strategies.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 4, 39, 42 and 75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 14, 2006.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 5-22, 24, 30-36, 38, 40, 41, 43-54, and 56-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for practice of the method using anti-MBL antibodies or antigen-binding fragments thereof, does not reasonably provide enablement for the broad recitation of "antibody fragment" or of individual CDR regions of an antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff (Proc Natl Acad Sci USA [1982] 79:1979-1983; U on form PTO-892). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function (see entire document).

MacCallum (J. Mol. Biol. [1996] 262:732-745; V on form PTO-892) analyzed a number of different antibodies for interactions with antigen and discloses that the CDR3s of the heavy and light chain dominate, however a number of residues outside the standard CDR definitions make antigen contacts (page 733, column 2 in particular) and non-contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (page 735, column 1 in particular).

Casset (Biochem. Biophys. Res. Comm. [2003] 307:198-205; W on form PTO-892) underscores the fact that not just one CDR is essential for antigen binding or maintaining the conformation of the antigen-binding site as shown in the case of the construction of a peptide mimetic of an anti-CD4 monoclonal antibody binding site by rational design. The peptide was designed with 27 residues formed by residues from 5 CDRs (see entire document). Casset discloses that although CDR H3 is at the center of most if not all antigen interactions, clearly other CDRs play an important role in the recognition process (page 199, column 1 in particular) and this is demonstrated in this work by using all CDRs except L2 and additionally using a framework residue located just before the H3 (page 202, column 1 in particular).

Wu (J. Mol. Biol. [1999] 294:151-162; X on form PTO-892) discloses that it is difficult to predict which framework residues serve a critical role in maintaining affinity and specificity due in part to the large conformational change in antibodies that accompany antigen binding but certain residues have been identified as important for maintaining conformation (page 152, column 1 in particular).

The instant specification does not disclose any "antibody fragment" that does not comprise an entire antigen-binding region or a single isolated CDR region that could be used in the claimed method.

Accordingly, in view of the limited guidance provided by the specification, the level of predictability in the art, the nature of the claimed invention and the undue experimentation required of one of ordinary skill in the art, it would require an undue amount of trial and error to practice the full scope of the invention and this is not sanctioned by the statute.

Claims 16 and 58 are included because the claims define the site on MBL, not the inhibitor.

Claims 17 and 59 are included because the claims define what competes with the inhibitor, not the structure of the inhibitor itself.

Conclusion

5. Claims 23, 25-29, 37, 55 and 68-74 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852.. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

F. Pierre VanderVegt, Ph.D. /PV/
Patent Examiner
June 22, 2007

David A Saunders

DAVID A. SAUNDERS
PRIMARY EXAMINER